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UNITED STATES DISTRICT COURT
DISTRICT OF UTAH

NUTRACEUTICAL CORPORATION and)
SOLARAY, INC.,)
)
Plaintiffs,)
)
v.)
)
ANDREW VON ESCHENBACH, M.D.,)
Commissioner, U.S. Food and Drug)
Administration, <u>et al.</u> ,)
)
Defendants.)

Case No. 2:04CV00409 PGC

DEFENDANTS' OPPOSITION TO PLAINTIFFS' MOTION FOR
SUMMARY JUDGMENT AND MEMORANDUM IN SUPPORT OF
CROSS-MOTION FOR SUMMARY JUDGMENT

INTRODUCTION

Pursuant to its authority under the Federal Food, Drug, and Cosmetic Act (FDCA) to "promulgate regulations for the efficient enforcement of [the statute]," 21 U.S.C. § 371(a), the Food and Drug Administration (FDA or agency) issued a regulation (Final Rule) that declares dietary supplements containing ephedrine alkaloids (EDS) to be adulterated under 21 U.S.C. § 342(f)(1)(A). See 69 Fed. Reg. 6788 (Feb. 11, 2004).¹ Under that section, Congress authorized FDA to protect the public health and safety by removing dietary supplements from the market when they present "a significant or unreasonable risk of illness or injury" under the recommended or ordinary conditions of use. 21 U.S.C. § 342(f)(1)(A). After compiling an extensive rulemaking record demonstrating the serious health risks – e.g., heart attack, stroke, and death – associated with the consumption of EDS, FDA acted pursuant to its authority under the FDCA to ban these products.

Plaintiffs, Nutraceutical Corp. and its subsidiary Solaray, Inc., (collectively, "Nutraceutical") brought suit in May 2004 to challenge the validity of the Final Rule. Nutraceutical alleged in its complaint that the Final Rule violates the Dietary Supplement Health and Education Act of 1994 (DSHEA)² and the Administrative Procedure Act (APA).³

¹ Final Rule Declaring Dietary Supplements Containing Ephedrine Alkaloids Adulterated Because They Present an Unreasonable Risk, codified at 21 C.F.R. § 119.1. For convenience, we cite to the original *Federal Register* pagination for all *Federal Register* publications referenced herein rather than to the pagination in the administrative record.

² Pub. L. No. 103-417, 108 Stat. 4325 (1994), amending the FDCA, 21 U.S.C. §§ 301 et seq.

³ Nutraceutical has dropped its argument that, in the alternative, the Final Rule is a taking of its property in violation of the Fifth Amendment, entitling it to compensatory damages.

Nutraceutical seeks to enjoin FDA from enforcing the Final Rule against its EDS product, which is labeled to contain 10 milligrams (mg) or less of ephedrine alkaloids per daily dose.

On April 13, 2005, the district court granted summary judgment to Nutraceutical, holding that FDA erred in interpreting DSHEA's "unreasonable risk" standard to require a risk-benefit analysis. Nutraceutical v. Crawford, 364 F. Supp. 2d 1310, 1319 (D. Utah 2005). The court also found that FDA failed to prove by a preponderance of the evidence that EDS containing a daily dose of 10 mg or less of ephedrine alkaloids present a significant or unreasonable risk of illness or injury. Id. at 1321.

The government appealed and, on August 17, 2006, the Tenth Circuit reversed. The appellate court held, "Congress unambiguously required the FDA to conduct a risk-benefit analysis under DSHEA" to determine whether EDS pose an unreasonable risk of illness or injury. Nutraceutical v. Von Eschenbach, 459 F.3d 1033, 1038 (10th Cir. 2006). The Tenth Circuit also held that FDA had demonstrated that EDS *at any dose level* pose an unreasonable risk of illness or injury and that, therefore, the agency was justified in banning EDS completely. Id. at 1040-43. The appellate court reversed the district court's decision and remanded the case for entry of judgment in favor of the government. Id. at 1043-44. On November 14, 2006, this Court granted summary judgment for the government and ordered further briefing on the two issues not reached by the district court. Docket No. 42.

On December 20, 2006, Nutraceutical filed a Motion for Summary Judgment, claiming that FDA violated the APA in two ways. First, Nutraceutical alleges that FDA did not give sufficient notice and opportunity to comment on the agency's use of a risk-benefit analysis to determine that EDS are adulterated. Second, Nutraceutical asserts that FDA was arbitrary and

capricious in prohibiting the marketing of EDS but "exempting" from the Final Rule other products – conventional foods and traditional Asian medicine – that contain ephedrine alkaloids.⁴

Nutraceutical's arguments raise no genuine issue of material fact and are unsupported by law. Indeed, many of these arguments are contrary to the Tenth Circuit's recent decision in this case, which Nutraceutical fails to cite anywhere in its brief. Nutraceutical is not entitled to the relief it seeks, and the Court should deny Plaintiffs' Motion for Summary Judgment. In addition, the Court should grant Defendants' Cross-Motion for Summary Judgment because the Final Rule complies with the notice-and-comment requirements of the APA, and FDA was not arbitrary and capricious in excluding non-dietary supplement products from the Final Rule.

STATEMENT OF UNCONTESTED MATERIAL FACTS

1. Following an alert issued by FDA advising consumers to stop using EDS because they are unsafe, the agency published the Final Rule declaring EDS to be adulterated because they present an unreasonable risk of illness or injury. Under the Final Rule, which went into effect on April 12, 2004, EDS can no longer be marketed in the United States. 69 Fed. Reg. at 6788.

2. FDA took this action based on the well-known, scientifically established pharmacology of ephedrine alkaloids, the peer-reviewed scientific literature on the effects of

⁴ The issues before this Court are also involved in other pending challenges to the Final Rule. See NVE, Inc. v. Department of Health and Human Services, No. 04-cv-0999 (D.N.J., filed Mar. 4, 2004), remanded after interlocutory appeal, 436 F.3d 182 (3d Cir. 2006); Hi-Tech Pharmaceuticals, Inc. v. Crawford, No. 1:05-cv-2083 (N.D. Ga., filed Aug. 10, 2005) (consolidated with No. 1:06-cv-0406 below); and two third-party complaints filed by Hi-Tech Pharmaceuticals in seizure actions brought by the government against its EDS products, United States v. 5 unlabeled boxes . . . of an article of food, No. 2:06-cv-0027 (W.D. Pa., filed Jan. 9, 2006) and United States v. 18 cases . . . of an article of food, No. 1:06-cv-0406 (N.D. Ga., filed Feb. 22, 2006).

ephedrine alkaloids, published case reports of adverse events, and the adverse events reported to the agency that have occurred in individuals using products containing ephedrine alkaloids, primarily dietary supplements. 69 Fed. Reg. at 6788. After evaluating the data, FDA concluded that all EDS, regardless of dose, pose a risk of serious adverse events. The Final Rule describes in detail the evidence showing that these products expose consumers to the consequences of increased blood pressure such as stroke, heart attack, and death, and increased morbidity and mortality from worsened heart failure and abnormal heart rhythms. See id. at 6800-18.

3. Dietary supplements, defined in 21 U.S.C. § 321(ff), are generally regulated as "foods" under the FDCA, as amended by DSHEA. Consequently, dietary supplement manufacturers are not required to demonstrate through clinical testing and other means that their products are safe and effective before marketing, nor are they subject to postmarketing product safety reporting requirements. 69 Fed. Reg. at 6798.

4. However, dietary supplements may not remain on the market after they have been found to pose an unreasonable risk of harm to consumers. When Congress enacted DSHEA in 1994, it instructed the federal government to "take swift action against [such] products that are unsafe or adulterated." DSHEA, Pub. L. No. 103-417, § 2(13), 108 Stat. at 4326.

5. Under DSHEA, a dietary supplement is adulterated – and thus may not be marketed in the United States, see 21 U.S.C. § 331(a), (b), (c), (k) – if, among other things, it "presents a significant or unreasonable risk of illness or injury under (i) conditions of use recommended or suggested in labeling, or (ii) if no conditions of use are suggested or recommended in the labeling, under ordinary conditions of use." 21 U.S.C. § 342(f)(1)(A).

6. "Congress unambiguously required the FDA to conduct a risk-benefit analysis under DSHEA" to determine whether EDS pose an unreasonable risk of illness or injury.

Nutraceutical, 459 F.3d at 1038.

7. Ephedrine alkaloids are a class of pharmacologically related chemical stimulants that include ephedrine, pseudoephedrine, norephedrine, methylephedrine, norpseudoephedrine, and methylpseudoephedrine. Ephedrine alkaloids occur naturally in some botanicals, but can also be synthetically created. 69 Fed. Reg. at 6789, 6794. In most botanical species of ephedrine alkaloids used commercially, ephedrine is typically the predominant alkaloid in the raw material. Id. at 6789.

8. In the United States, EDS have been labeled and used primarily to lose weight and enhance energy and athletic performance. Id. at 6789.

9. In 1995, soon after the passage of DSHEA, FDA began examining the potential public health problems associated with EDS. Id. at 6790.

10. By January 1997, FDA had received over 800 reports of serious adverse events (including death) associated with EDS and other scientific evidence raising major concerns about the safety of such products. 62 Fed. Reg. 30,678, 30,679-91 (June 4, 1997).

11. Later that year, pursuant to its FDCA rulemaking authority (21 U.S.C. § 371(a)), FDA initiated a rulemaking proceeding in which it solicited public comment on proposed labeling and formulation restrictions for EDS. 62 Fed. Reg. at 30,678. FDA also made public the administrative record containing some 221 scientific and other references, as well as the adverse event reports (AERs) it had received. Id. at 30,713-17, 30,718-24.

12. The proposed rule relied on 21 U.S.C. § 342(f)(1)(A) as FDA's authority for regulating EDS. See, e.g., 62 Fed. Reg. at 30,693, 30,695, 30,696.

13. After receiving additional AERs and the results of chemical analyses of several EDS associated with such reports, and discovering some inadvertent omissions in the administrative record, FDA reopened the period for public comment and made the supplemented record publicly available. 62 Fed. Reg. 48,968 (Sept. 18, 1997).

14. In April 2000, FDA issued a notice withdrawing part of its proposed rule to regulate EDS. 65 Fed. Reg. 17,474 (Apr. 3, 2000). This action was taken in response to comments received by FDA on the proposed restrictions on EDS, as well as an August 1999 report by the General Accounting Office (GAO) recommending that FDA "provide stronger evidence on the relationship between the intake of dietary supplements containing ephedrine alkaloids and the occurrence of adverse reactions that support the proposed dosing level and duration of use limits." Id. at 17,475.

15. FDA therefore decided to "reconsider, with public input, whether any dietary ingredient level or duration of use limit for [EDS] is appropriate or whether alternative measures should be considered." Id. The agency stressed, however, that its action withdrawing certain portions of the proposal "does not limit [its] discretion to initiate enforcement actions with respect to [EDS]" if warranted. Id. at 17,476.

16. At the same time, FDA updated the public docket for the proposed rule, 65 Fed. Reg. 17,509 (Apr. 3, 2000), and announced the availability of additional EDS-related AERs and related scientific information. 65 Fed. Reg. 17,510 (Apr. 3, 2000). The agency also invited comment and participation at a public forum to discuss the new documentation, and it actively

"encourage[d] interested persons" to submit "new usage data, and new scientific information, including clinical trials sponsored by manufacturers, that support[] the safety of [EDS]," as well as "any other information the submitter believes is relevant to assessing the safety" of these products. Id. at 17,512.

17. In response to a number of requests, FDA extended, and later again reopened, that comment period. 65 Fed. Reg. 32,113 (May 22, 2000); 65 Fed. Reg. 46,721 (July 31, 2000). The available information concerning the safety of EDS was discussed at a public meeting held in August 2000. See 65 Fed. Reg. 43,021 (July 12, 2000).

18. After "more scientific evidence [came] to light concerning the risks posed by ephedrine alkaloids, including approximately 17,000 adverse event reports," FDA invited public comment on its EDS proposal for the fifth time. 68 Fed. Reg. 10,417, 10,418 (Mar. 5, 2003).

19. The agency proposed a warning statement, consistent with the new scientific studies that it had received and that were identified in the notice, including a review of the scientific literature by the RAND Corporation, which was under contract with the Department of Health and Human Services. Id. at 10,418-19, 10,420. FDA also stated its intent to consider whether, given currently available information, it "should determine that [EDS] present a 'significant or unreasonable risk of illness or injury under conditions of use recommended or suggested in labeling, or if no conditions of use are suggested or recommended in the labeling, under ordinary conditions of use.'" Id. at 10,417; see also id. at 10,419 (citing 21 U.S.C. § 342(f)(1)(A), the statutory standard for adulteration), 10,420 (advising that FDA will "take any other action" determined to be appropriate to protect the public health and safety).

20. While the rulemaking was pending, FDA received three petitions containing various proposals concerning how EDS should, or should not, be regulated. One petition, filed by Public Citizen in September 2001, requested that FDA (i) declare that EDS present "a significant or unreasonable risk of illness or injury," and (ii) ban all production and sale of these products. See 69 Fed. Reg. at 6792. Public Citizen's petition was filed in FDA's public docket, notice of its filing was given on FDA's website, and any interested person was free to submit comments on it. See 21 C.F.R. § 10.30(c), (d).

21. The agency ultimately received more than 48,000 comments from the public and developed a 133,000-page record, which includes scientific information documenting the risks associated with EDS. The administrative record includes 161 references cited in the Final Rule, many of which are scientific studies. 69 Fed. Reg. at 6792, 6849-53.

22. On February 11, 2004, FDA published the Final Rule that declares all EDS to be adulterated under 21 U.S.C. § 342(f)(1)(A) because such products present an "unreasonable risk of illness or injury" under the conditions of use suggested in labeling or, in the absence of such labeling, under ordinary conditions of use. 69 Fed. Reg. at 6788.

23. Evaluating the evidence FDA developed in accordance with a risk-benefit analysis, the agency concluded that all EDS pose an unreasonable risk: "The data do not indicate that these products provide a health benefit sufficient to outweigh the risks" of cardiac arrhythmias, worsened heart failure, and increased blood pressure resulting in heart attack, stroke, and death, from short- and long-term use of EDS. 69 Fed. Reg. at 6789.

24. In particular, FDA determined that "[t]he best clinical evidence for a benefit [from using EDS] is for weight loss, but even there the evidence supports only a modest short-term

weight loss [no more than 6 months], insufficient to positively affect cardiovascular risk factors or health conditions associated with being overweight or obese." Id. at 6789.

25. The agency further concluded that: (a) there is no scientific data to show that short-term weight loss results in improved health outcomes; (b) only long-term weight loss in overweight or obese individuals has been shown to reduce the risk of morbidity and mortality; (c) there are no appropriate, well-designed studies showing that EDS produce long-term weight loss (i.e., weight loss for more than 6 months); and (d) therefore, the short-term, modest weight loss achieved with botanical ephedrine alkaloids is insufficient to have a positive effect on cardiovascular risk factors or health conditions associated with being overweight or obese. Id. at 6818-21, 6825-26; see also id. at 6821-22, 6826-27 (discussion and rejection of claims for enhanced athletic performance, eased breathing, and other asserted benefits of EDS use).

26. FDA balanced the foregoing limited benefits against the known and likely risks of short-and long-term EDS use. The agency found that individuals with coronary artery disease or heart failure – many of whom may not know they have these underlying illnesses – are at increased risk of serious adverse health effects from EDS, including worsening of the underlying illnesses and death. Id. at 6802.

27. FDA found that EDS can cause cardiac arrhythmias, even when the product is ingested at doses recommended by manufacturers over a short course (one or a few doses). FDA stated that, in fact, the occurrence of an arrhythmic event triggered by EDS does not require prolonged EDS use, but represents a risk associated with each use, including the first. Id. at 6789, 6800-02, 6805-06.

28. In addition, FDA found that EDS also raise blood pressure. A sustained increase in blood pressure in any population will increase the risk of heart attack, stroke, and death. Id. at 6789, 6801-02. The risk of harmful consequences from elevated blood pressure increases the longer the blood pressure remains elevated, and these serious adverse health effects are likely to occur sooner in individuals with hypertension, a condition that is highly prevalent and often undiagnosed in the United States. Id.

29. FDA found that, with continued EDS use, the risk of heart attacks, stroke, and death to the general population – even people with "normal" blood pressure – also increases because of a sustained elevation in blood pressure. Id. at 6789, 6800-09; see also id. at 6809-18 (discussing other safety issues and a total of approximately 19,000 adverse event reports received by the agency).

30. FDA therefore determined that the risks of EDS use outweigh the benefits. Id. at 6825-27.

31. FDA demonstrated that EDS at any dose level pose an unreasonable risk of illness or injury and was justified in banning EDS completely. Nutraceutical, 459 F.3d at 1040-43.

32. The agency accordingly promulgated 21 C.F.R. § 119.1, stating that EDS are adulterated under 21 U.S.C. § 342(f)(1)(A). The regulation took effect on April 12, 2004. 69 Fed. Reg. at 6788, 6853.

33. FDA considered other regulatory restrictions and actions to protect consumers from the risks posed by EDS – primarily warning statements on dietary supplement labeling and prohibitions on dietary supplements that combine ephedrine alkaloids with other stimulants, along with various alternatives suggested in the public comments, such as dosage limits, self-

regulation, public education, and targeted enforcement actions. The agency explained, however, that none of those alternatives would adequately protect the public health from the serious dangers posed by EDS. Id. at 6827-30.

34. For example, labeling recommending a limit on the duration of product use cannot "provide adequate protection because adverse events sometimes occur after the first use or in the first few days." Id. at 6829. In addition, because no safe dose of ephedrine alkaloids in dietary supplements can be identified, "dose limitations cannot change the unfavorable risk-benefit ratio of these products." Id. Even a dose as low as 1.5 mg every 4 hours (9 mg per day) "would produce cardiovascular effects that may be dangerous alone, or in association with other risk factors." Id. at 6805.

35. In response to public comments, FDA explained that the Final Rule does not apply to ephedrine alkaloid-containing products that are not dietary supplements. For example, ephedrine alkaloids added to conventional foods are generally considered to be unsafe "food additives," see 21 U.S.C. § 321(s), which would render the food adulterated under *different* provisions of the FDCA, see id. §§ 342(a)(2)(C), 348. 69 Fed. Reg. at 6793. The Final Rule also does not apply to over-the-counter (OTC) or prescription drugs containing ephedrine, which are subject to the stringent statutory and regulatory requirements that pertain to all drugs. See 69 Fed. Reg. at 6793, 6800, 6811. FDA noted that OTC products containing ephedrine have demonstrated benefits in the treatment and mitigation of disease. The benefits of these products outweigh the risks and justify their use despite their risks. Id. at 6809-11.

**RESPONSE TO NUTRACEUTICAL'S STATEMENT
OF UNDISPUTED MATERIAL FACTS**

Defendants have no objection to the statements of fact contained in paragraphs 2, 5, 6, 9, 14, 15, 17, 19, 22, 24, 25, 26, 28, 29, 41, 42, and 43 of the Memorandum of Points and Authorities in Support of Plaintiffs' Motion for Summary Judgment. Although Defendants do not agree with statements made in the remaining paragraphs, these objections do not raise triable issues of fact because the objections involve allegations of immaterial facts that cannot be genuinely disputed or issues of law. Nevertheless, Defendants make the following objections:

1. The allegations in paragraph 1 are denied to the extent that they suggest that the Ephedra genus of plants has been used as a conventional food for thousands of years. As stated in the Final Rule, several Ephedra species have a long history of use in traditional Asian medicine. 69 Fed. Reg. at 6793-94.

3. Defendants object to the allegations in paragraph 3 to the extent that Nutraceutical supports the allegations by relying on material outside of the administrative record in this case (i.e., Exhibit A).

4. Defendants deny Nutraceutical's characterization of the FDA's Final Rule in paragraph 4. The Final Rule explicitly applies only to dietary supplements containing ephedrine alkaloids. Defendants further object to the allegations in paragraph 4 to the extent that Nutraceutical supports the allegations by relying on material outside of the administrative record in this case (i.e., Exhibit A).

7. Defendants deny Nutraceutical's characterizations of the FDA's 1997 Proposed Rule in paragraph 7. The 1997 Proposed Rule states:

Following the August 1996 meeting of the Food Advisory Committee, the agency completed its review of the majority of the AER's associated with these products and reviewed the discussions and the recommendations of the Food Advisory Committee, the scientific literature, the views expressed in public comments, and other data. Based on this information, the agency has tentatively concluded that use of ephedrine alkaloids raises important public health concerns, that the risks these substances create are potentially very serious, and that action must be taken to protect the public health.

62 Fed. Reg. at 30680. The scientific evidence included "the known pharmacology of ephedrine alkaloids, numerous case reports published in the scientific literature, and published findings from clinical studies investigating the use of ephedrine in the treatment of obesity. Id.

8. Defendants deny Nutraceutical's characterizations of the FDA's 1997 Proposed Rule in paragraph 8. The paragraph in the 1997 Proposed Rule immediately following the material quoted by Nutraceutical states:

FDA recognizes, however, that this 10-mg level is also subject to some uncertainty because of such factors as intra-assay variabilities (i.e., difference in analytical results from one run to the next with the same method), natural variabilities in the alkaloid content of botanical ingredients, variations in formulation levels from batch to batch, and inaccuracies in the amounts reported to be taken by consumers. When these sources of variability are considered, given that they are likely to be additive, the range around the 10 mg per serving estimated intake can be expected to deviate by ± 10 to 20 percent. Thus, FDA tentatively concludes that the life-threatening adverse events associated with the use of ephedrine alkaloids can reasonably be expected to occur at intake levels as low as 8 to 9 mg ephedrine alkaloids per serving. However, given the limitations in the available data, the agency requests comments on whether it is more appropriate to focus on the 10 mg level.

62 Fed. Reg. at 30693.

10. Defendants deny Nutraceutical's characterizations of the FDA's 1997 Proposed Rule in paragraph 10. See infra at III.A. under "Argument."

11. Defendants deny Nutraceutical's characterizations of the FDA's 1997 Proposed Rule in paragraph 11. See infra at III.A. under "Argument."

12. Defendants deny Nutraceutical's characterizations of the FDA's 1997 Proposed Rule in paragraph 12. See infra at III.A. under "Argument."

13. Defendants deny Nutraceutical's characterizations of the FDA's 1997 Proposed Rule in paragraph 13. See infra at III.A. under "Argument."

16. The allegations in paragraph 16 are denied. In its 1999 report, GAO concluded that FDA was justified in determining that the number of AERs relating to EDS warranted the agency's attention and consideration of steps to address safety issues, but recommended that FDA "provide stronger evidence on the relationship between the intake of [EDS] and the occurrence of adverse reactions that support the proposed dosing level and duration of use limits." 65 Fed. Reg. at 17475.

18. Defendants object to the allegations in the second sentence in paragraph 18 because they reflect conclusions of law relating to the meaning of the statutory term "unreasonable risk."

20. Defendants object to the allegations in paragraph 20 because they reflect conclusions of law relating to the meaning of the statutory term "unreasonable risk."

21. Defendants object to the allegations in paragraph 21 because they reflect conclusions of law relating to the meaning of the statutory term "unreasonable risk." Defendants also deny Nutraceutical's characterizations of the FDA's 1997 Proposed Rule in the third sentence in paragraph 21. See infra at III.A. under "Argument."

23. The allegations in paragraph 23 are denied to the extent that they suggest that FDA did not address comments submitted by Nutraceutical during this rulemaking. In the Final Rule,

FDA explicitly responded to comments it received that “expressed the view that low doses of ephedrine alkaloids in dietary supplements do not pose a safety concern and should remain on the market.” 69 Fed. Reg. at 6805; see id. at 6828-29 (responding to comments suggesting dose limitations (among other measures) to reduce the risk of adverse events).

27. Defendants object to the allegations in paragraph 27 because Nutraceutical supports the allegations by relying on material outside of the administrative record in this case (i.e., Exhibit E, the affidavit of Jeffrey A. Hinrichs). Defendants also deny Nutraceutical’s characterizations of the FDA’s 1997 Proposed Rule and subsequent *Federal Register* notices in paragraph 27. See infra at III.A. under “Argument.”

30. Defendants deny Nutraceutical’s characterizations of the FDA’s Final Rule in paragraph 30. Defendants respectfully refer the Court to the referenced language of the Final Rule, which is the best evidence of its contents.

31. Defendants deny Nutraceutical’s characterizations of the FDA’s Final Rule in paragraph 31. Defendants respectfully refer the Court to the referenced language of the Final Rule, which is the best evidence of its contents.

33. Defendants deny Nutraceutical’s characterizations of the FDA’s Final Rule in paragraph 33. Defendants respectfully refer the Court to the referenced language of this Final Rule, which is the best evidence of its contents.

34. Defendants deny Nutraceutical’s characterizations of the FDA’s Final Rule in paragraph 34. The Final Rule states: “Some dietary supplements containing ephedrine alkaloids are promoted for disease uses, e.g., to treat obesity. In such instances, [FDA] can and ha[s] taken action against certain dietary supplement products as drugs.” 69 Fed. Reg. at 6795.

35. The allegations in paragraph 35 are denied to the extent that they suggest that FDA did not address comments submitted by Nutraceutical during this rulemaking. In the Final Rule, FDA explicitly responded to comments it received that “expressed the view that low doses of ephedrine alkaloids in dietary supplements do not pose a safety concern and should remain on the market.” 69 Fed. Reg. at 6805; see id. at 6828-29 (responding to comments suggesting dose limitations (among other measures) to reduce the risk of adverse events). Defendants further object to the allegations in paragraph 35 to the extent that Nutraceutical supports the allegations by relying on material outside of the administrative record in this case (i.e., Exhibit F).

36. The allegations in paragraph 36 are denied. As recognized by the United States Court of Appeals for the Tenth Circuit in its recent opinion in this case, FDA relied upon “sufficiently probative” evidence demonstrating that EDS posed an unreasonable risk at any dose level. Nutraceutical, 459 F.3d at 1043. Defendants further object to the allegations in paragraph 36 to the extent that Nutraceutical supports the allegations by relying on material outside of the administrative record in this case (i.e., Exhibit F).

37. The allegations in paragraph 37 are denied. As recognized by the United States Court of Appeals for the Tenth Circuit in its recent opinion in this case, FDA relied upon “sufficiently probative” evidence demonstrating that EDS posed an unreasonable risk at any dose level. Nutraceutical, 459 F.3d at 1043. Defendants further object to the allegations in paragraph 37 to the extent that Nutraceutical supports the allegations by relying on material outside of the administrative record in this case (i.e., Exhibits F, G).

38. Defendants object to the allegations in paragraph 38 because they reflect conclusions of law relating to the meaning of the statutory term “unreasonable risk.”

39. Defendants object to the allegations in paragraph 39 to the extent that Nutraceutical supports the allegations by relying on material outside of the administrative record in this case (i.e., Exhibits G).

40. Defendants deny Nutraceutical's characterization of the FDA's Final Rule in paragraph 40. Defendants respectfully refer the Court to the referenced language of this Final Rule, which is the best evidence of its contents. The Final Rule also states that FDA "conclude[d], based on available science, that all dietary supplements containing ephedrine alkaloids present an unreasonable risk of illness or injury, regardless of how they are formulated or labeled, because the risks outweigh any benefits that may result from use of the products. Therefore, [FDA] may issue a rule finding the entire class of products adulterated." 69 Fed. Reg. 6798.

ARGUMENT

I. SUMMARY JUDGMENT STANDARD

Summary judgment is appropriate "if the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to judgment as a matter of law." Fed. R. Civ. P. 56; Celotex Corp. v. Catrett, 477 U.S. 317, 322 (1986); see also Anderson v. Liberty Lobby, 477 U.S. 242 (1986); Rakity v. Dillon Cos., 302 F.3d 1152, 1157 (10th Cir. 2002). The movant may demonstrate lack of a genuine issue of material fact either by demonstrating that the non-movant's evidence is not sufficient to establish an essential element of his or her claim, or by submitting affirmative evidence that negates an essential element of the claim. Celotex, 477 U.S. at 322. A fact is material if, "under the governing law, it could have an

effect on the outcome of the lawsuit." Rakity, 302 F.3d at 1157. An issue of material fact is genuine only if the non-movant presents facts such that a reasonable trier of fact could find in favor of the non-movant. Planned Parenthood of the Rocky Mountains Services v. Owens, 287 F.3d 910, 916 (10th Cir. 2002) (citation and quotation omitted).

A party may not defeat a motion for summary judgment by simply showing that there is some metaphysical doubt as to the material facts. Matsushita Elec. Indus. Co. v. Zenith Radio Corp., 475 U.S. 574, 586 (1986). Once the movant shows the absence of a genuine issue of material fact, the non-movant cannot merely rest upon his or her pleadings, "but must set forth specific facts showing that there is a genuine issue for trial." Cudjoe v. Independent School Dist. No. 12, 297 F.3d 1058, 1062 (10th Cir. 2002); (quoting Bullington v. United Air Lines, Inc., 186 F.3d 1301, 1313 (10th Cir. 1999); see also Matsushita, 475 U.S. at 586.⁵

The government is entitled to summary judgment here because Plaintiffs have not identified any material factual issues (indeed, most of their challenges are legal), and the government is entitled to judgment as a matter of law. See Fed. R. Civ. P. 56(c).

II. THE FINAL RULE COMPLIES WITH THE APA'S NOTICE AND COMMENT PROCEDURES AND IS NOT ARBITRARY AND CAPRICIOUS

FDA's promulgation of the Final Rule was lawful and consistent with APA requirements. FDA provided the public with adequate notice and opportunity for comment when promulgating the Final Rule, and the Final's Rule application to EDS, but not to ephedrine alkaloid-containing

⁵ The scope of the Court's review of the Final Rule is limited to the administrative record. Because Nutraceutical's motion is styled as a motion for summary judgment, Defendants use the same format in their opposition and cross-motion. Defendants recognize that, in the 10th Circuit, judicial review of agency action under the Administrative Procedure Act (APA) is to be processed as an appeal. See Olenhouse v. Commodity Credit Corp., 42 F.3d 1560, 1580 (10th Cir. 1994). In this review, it is inappropriate for the Court to consider matters outside of the administrative record See Olenhouse, 42 F.3d at 1579-80.

products that are not dietary supplements, is consistent with the statutory scheme and not arbitrary or capricious. As explained in detail below, FDA has met its burden to show that the Final Rule was lawfully promulgated.

A. The Final Rule Complies With Notice And Comment Rulemaking

The APA requires agencies to publish notice of proposed rulemaking in the *Federal Register*. See 5 U.S.C. § 553(b). The notice must include, among other things, either the terms or substance of the proposed rule or a description of the subjects and issues involved. See 5 U.S.C. § 553(b)(3); 21 C.F.R. § 10.40(b)(1)(viii). After publishing notice, the agency must give interested persons an opportunity to participate in the rulemaking through submission of written views, arguments, or data, and must consider the comments received. See 5 U.S.C. § 553(c).

"[T]he notice need not specifically identify 'every precise proposal which [the agency] may ultimately adopt as a final rule.'" Chemical Mfrs. Ass'n v. EPA, 870 F.2d 177, 203 (5th Cir. 1989) (quoting United Steelworkers of Am. v. Schuylkill Metals, 828 F.2d 314, 317 (5th Cir. 1987) (citations omitted)). Notice is adequate under the APA so long as it facilitates meaningful participation by the public by "'fairly appris[ing] interested persons' of the nature of the rulemaking." United Steelworkers of Am. v. Marshall, 647 F.2d 1189, 1221 (D.C. Cir. 1980) (quoting American Iron & Steel Inst. v. EPA, 568 F.2d 284, 293 (3d Cir. 1977)).

Moreover, agencies "undoubtedly [have] authority to promulgate a final rule that differs in some particulars from its proposed rule [because] . . . '[a] contrary rule would lead to the absurdity that . . . the agency can learn from the comments on its proposals only at the peril of starting a new procedural round of commentary.'"⁶ Small Refiner Lead Phase-Down Task Force

⁶ "That an agency changes its approach to the difficult problems it must address does not signify the failure of the administrative process. Instead, an agency's change of course, so long as

v. EPA, 705 F.2d 506, 546-47 (D.C. Cir. 1983) (quoting International Harvester Co. v. Ruckelshaus, 478 F.2d 615, 632 n.51 (D.C. Cir. 1973)); Beirne v. Sec'y of Dep't Agric., 645 F.2d 862, 865 (10th Cir. 1981). In determining the adequacy of notice, the court should strike a balance between the agency's need to change the final rule based on comments, new information, or further consideration of the issue, and the public's right to participate meaningfully in the rulemaking. See Small Refiner, 705 F.2d at 546-47. In striking this balance, courts apply the logical outgrowth test. See South Terminal Corp. v. EPA, 504 F.2d 646 (1st Cir. 1974). "The question is typically whether the agency's final rule so departs from its proposed rule as to constitute more surprise than notice." Air Transp. Ass'n of Am. v. FAA, 169 F.3d 1, 7 (D.C. Cir. 1999). Put another way, the test is whether the regulated party "should have anticipated that such a requirement might be imposed." Small Refiner, 705 F.2d at 549.

Here, the public had abundant notice that FDA proposed to regulate EDS under 21 U.S.C. § 342(f)(1)(A), and that, after it had examined the practicability of various regulatory options relating to dose levels, label restrictions, warnings, and enforcement actions, FDA might adopt any degree of regulation necessary to address the safety concerns about the products. The 1997 Proposed Rule and subsequent *Federal Register* notices re-opening the comment period alerted all interested persons that the agency might adopt a final rule that included any or all of these strategies to regulate EDS under 21 U.S.C. § 342(f)(1)(A). The public had ample notice and opportunity for meaningful participation in the process. The Final Rule was the culmination of a

generally consistent with the tenor of its original proposals, indicates that the agency treats the notice-and-comment process seriously" American Med. Assoc. v. United States, 887 F.2d 760, 767 (7th Cir. 1989).

seven-year rulemaking that included five separate comment periods during which the agency received over 48,000 comments. See 69 Fed. Reg. at 6789-93.

The 1997 Proposed Rule and subsequent *Federal Register* notices provided adequate notice of the Final Rule's subject matter and potential outcome. The substantive issue involved in both the proposed and Final Rule is the same – whether the products were adulterated and, if so, whether the risks associated with EDS could be managed with restrictions on marketing. Compare 62 Fed. Reg. at 30,697-30,703 (1997 Proposed Rule) with 69 Fed. Reg. at 6798-6807 (Final Rule). The major difference between the 1997 Proposed Rule and the Final Rule is the extent of the regulatory restrictions.

The relevant *Federal Register* notices illustrate FDA's logical and transparent progression to the Final Rule. From 1997 until the Final Rule was promulgated in 2004, FDA several times gave notice that it was considering the risks of EDS and whether the agency should find EDS adulterated under 21 U.S.C. § 342(f)(1)(A). Like the Final Rule, the Proposed Rule relied on 21 U.S.C. § 342(f)(1)(A) as FDA's authority for regulating EDS. See, e.g., 62 Fed. Reg. at 30,693, 30,695, 30,696; see infra at III.A. In its April 2000 notice withdrawing parts of the 1997 Proposed Rule, FDA requested comments and relevant information regarding its ongoing safety assessment. See generally 65 Fed. Reg. 17,474 (Apr. 3, 2000). Furthermore, in March 2003, FDA stated that it was seeking comments specifically on whether EDS presented an unreasonable risk of illness or injury under 21 U.S.C. § 342(f)(1)(A).⁷

⁷ See 68 Fed. Reg. 10,417, 10,419 (Mar. 5, 2003):

FDA also intends to consider, to the extent possible, whether in light of current information FDA should determine that [EDS] present a "significant or unreasonable risk of illness or injury under conditions of use recommended or suggested in labeling, or if no conditions of use are

Comments advanced during the rulemaking also demonstrate that FDA adequately foreshadowed its decision to declare EDS adulterated under 21 U.S.C. § 342(f)(1)(A). Any notion that the public received inadequate notice is contradicted by many comments – including Nutraceutical's (see infra at n.16) – in the record. In fact, many comments specifically discussed conducting a risk-benefit analysis to determine unreasonable risk.⁸ Although comments are not determinative of proper notice and comment procedures in and of themselves, comments regarding the possibility of finding EDS adulterated under 21 U.S.C. § 342(f)(1)(A) using a risk-benefit analysis are a strong indicator that the public in fact received adequate notice of the Final Rule. See Shell Oil Co. v. EPA, 950 F.2d 741, 757 (D.C. Cir. 1991) (noting that comments on the issue are evidence that the public received adequate notice).

B. FDA's Regulation Of EDS Under The Final Rule Is Consistent With The FDCA

The APA reflects the principles of Chevron and "provides that 'agency action must be set aside if the action was "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law" or if the action failed to meet statutory, procedural, or constitutional requirements.'" Valley Cmty. Pres. Comm'n v. Mineta, 373 F.3d 1078, 1084 (10th Cir. 2004) (quoting Citizens to Preserve Overton Park v. Volpe, 401 U.S. 402, 414 (1971) (citing 5 U.S.C. § 706(2)(A), (B), (C), (D))). A court's review under this standard is narrow and deferential.

suggested or recommended in the labeling, under ordinary conditions of use." (see 21 U.S.C. § 342(f)(1)(A)).

⁸ See, e.g., Comment from the Ephedra Education Council discussing benefits at length and stating, "[EDS] side effects, when evaluated in a risk/benefit analysis, are few and minor in comparison to the public health benefit that results from ephedra supplement consumption," A.R. 102078-102101 at 102087-91, attached at Exh. A; Comment submitted on behalf of several members of the dietary supplement industry stating "[a] conclusion as to the safety of a product requires a risk/benefit analysis," A.R. 076164-076194 at 076179-80, attached at Exh. B.

Overton Park, 401 U.S. at 416-17. The agency's action must be upheld "if it has articulated a rational basis for the decision and has considered relevant factors." Slingluff v. Occupational Safety & Health Review Comm'n, 425 F.3d 861, 866 (10th Cir. 2005) (citing Mountain Side Mobile Estates P'ship v. Sec'y of HUD, 56 F.3d 1243, 1250 (10th Cir. 1995)). Under the APA, regulations are presumed to be valid, and the agency is entitled to deference. Nutraceutical, 459 F.3d at 1038. As discussed below, the scope of the Final Rule is consistent with the statutory provisions of DSHEA, and FDA was reasonable in promulgating the Final Rule to focus on dietary supplements and implement the dietary supplement adulteration provision.

Under DSHEA, Congress authorized FDA to remove a dietary supplement from the market if, among other things, it "presents a significant or unreasonable risk of illness or injury under -- (i) conditions of use recommended or suggested in labeling, or (ii) if no conditions of use are suggested or recommended in the labeling, under ordinary conditions of use." 21 U.S.C. § 342(f)(1)(A). Section 342(f)(1) explicitly applies only to dietary supplements and dietary ingredients in dietary supplements. By definition, dietary supplements are not represented for use as conventional foods. See 21 U.S.C. § 321(ff)(2)(B) (defining "dietary supplement," in part, as a product that "is not represented for use as a conventional food or as a sole item of a meal or the diet").

The Final Rule, which is based on § 342(f)(1)(A), thus applies to EDS, but not to ephedrine alkaloid-containing products that are not dietary supplements. Far from being arbitrary and capricious, the exclusion of products that are not dietary supplements from the Final Rule is

consistent with the statutory provisions of DSHEA. Indeed, as a matter of law, the Final Rule does not and could not apply to conventional foods.⁹

DSHEA amended the FDCA to add a number of provisions that not only permit, but require, FDA to regulate dietary supplements differently from conventional foods. See e.g., 21 U.S.C. §§ 342(f) (adulteration provisions applicable only to dietary supplements), 343(q)(5)(F) (special nutrition labeling requirements for dietary supplements), 343(s) (misbranding provisions applicable only to dietary supplements). Had Congress intended FDA to regulate foods and dietary supplements identically, there would have been no need to create statutory provisions applicable specifically to dietary supplements. Where, as here, Congress expressly provided that dietary supplements be subject to the "unreasonable risk" standard that does not apply to conventional foods, FDA may implement the unreasonable risk adulteration provision without being arbitrary and capricious. Cf. Nutraceutical, 459 F.3d. at 1043 (holding that, in the context of justifying a total ban of EDS, "FDA was not arbitrary or capricious in its Final Rule").

In addition, although the dietary supplement adulteration provision does not apply to conventional foods, that does not necessarily mean that conventional foods containing ephedrine alkaloids are lawful under the FDCA.¹⁰ For example, substances intentionally added to a

⁹ The same is true for drug products – the Final Rule is inapplicable to them as a matter of law. 69 Fed. Reg. at 6793. OTC and prescription drugs containing ephedrine are subject to the stringent statutory and regulatory requirements that pertain to all drugs. See id. at 6793, 6800, 6811.

¹⁰ In its Motion for Summary Judgment, Nutraceutical argues that FDA has elevated form over substance by regulating EDS under the Final Rule, but exempting ephedrine alkaloid-containing conventional foods or traditional Asian medicines from such regulation. Pls. Mem. at 15-16. It appears that, in Nutraceutical's view, exempting products that are not dietary supplements from a dietary supplement regulation (i) is irrational, and (ii) makes the exempted products legal under the FDCA. As discussed in this section, Nutraceutical is wrong on both points.

conventional food that contains other ingredients are food additives under 21 U.S.C. § 321(s), unless they are generally recognized as safe (GRAS) or fall under another exception to the food additive definition. Because ephedrine alkaloid-containing botanicals are not GRAS, they would generally be considered unsafe food additives when used in a conventional food. See 21 U.S.C. § 348(a); 69 Fed. Reg. at 6793. A food that contains an unsafe food additive is adulterated under 21 U.S.C. § 342(a)(2)(C) and cannot be legally marketed under the FDCA.¹¹

III. NUTRACEUTICAL'S ARGUMENTS IN SUPPORT OF ITS MOTION FOR SUMMARY JUDGMENT ARE BASELESS

A. The 1997 Proposed Rule Did Not Create A So-Called "Consolidated Standard" Of Adulteration

Nutraceutical incorrectly contends that FDA promulgated the Final Rule without adequate notice and opportunity for comment. When Nutraceutical initially challenged the Final Rule, it argued that FDA did not give notice of its intent to use a risk-benefit analysis to determine unreasonable risk. This meritless argument is now foreclosed, however, because the Tenth Circuit has held that DSHEA's "unreasonable risk" standard *unambiguously* requires a product's risks to be balanced against its benefits. See Nutraceutical, 459 F.3d at 1038. In an effort to side-step the Tenth Circuit's decision, Nutraceutical has now attempted to make a different argument by asserting that FDA failed to give notice of a *change* in its *existing* policy from that which was articulated in the 1997 Proposed Rule to the Final Rule's implementation of DSHEA's adulteration provision, 21 U.S.C. § 342(f)(1)(A). See Pls. Mem. at 5-8. This new

¹¹ To the extent that traditional Asian medicines meet the definition of a drug – an article intended to be used in the diagnosis, cure, mitigation, treatment, or prevention of disease, 21 U.S.C. § 321(g) – they are properly regulated as drugs. A traditional Asian medicine that contains ephedrine alkaloids and that is a drug under the FDCA would be an unapproved new drug, which cannot be legally marketed. See, e.g., 21 U.S.C. § 331(d).

argument is foreclosed by this Court's Order, which states that "the parties shall submit a proposed briefing schedule for the filing of dispositive motions on the *remaining issues* in this case."¹² Docket No. 42 (emphasis added). This new argument is also unfounded.¹³

Nutraceutical claims that, in the 1997 Proposed Rule, the agency expressed its intent to rely on a "Consolidated Standard," an "amalgamation" of provisions in the FDCA, to evaluate whether EDS are adulterated. Pls. Mem. at 6-8. Nutraceutical further alleges that FDA combined different FDCA adulteration standards – i.e., injurious to health (§ 342(a)(1)), significant risk (§ 342(f)(1)(A)), and unreasonable risk (§ 342(f)(1)(A)) – to create a new statutory standard, which it calls a "Consolidated Standard," that represents a "harmonious whole" between dietary supplements and conventional foods. Pls. Mem. at 7. This claim is not tethered to reality. Therefore, it should be ignored, as should Nutraceutical's baseless conclusion that, in promulgating the Final Rule, FDA did not follow the "Consolidated Standard" it erroneously claims FDA created in the 1997 Proposed Rule (see Pls. Mem. at 9).

The language of the Proposed Rule demonstrates that the agency viewed the "injurious to health" and "significant or unreasonable risk" standards as independent bases for declaring EDS to be adulterated. Rather than presenting a "Consolidated Standard," in the 1997 Proposed Rule, the agency relied on two independent provisions of the FDCA that separately gave FDA authority

¹² In its Memorandum in Support of Plaintiffs' Motion for Order Renewing Remaining Causes of Action, Nutraceutical stated that the district court did not rule on its "APA claim that the Final Rule adopted a legislative 'risk-benefit' standard without advance notice and opportunity for comment as required by the APA." Docket No. 40 at 1; see also Cmplt ¶ 46.

¹³ Nutraceutical also challenges the scientific support for the Final Rule and the quantum of evidence on which FDA relied. Pls. Mem. at 9-10, 12. The issue, which was resolved by the Tenth Circuit, is not before the Court here. See Nutraceutical, 459 F.3d at 1043.

find EDS adulterated. Nutraceutical is simply incorrect in asserting that FDA established an "interpretive consolidation" of 21 U.S.C. §§ 342(a)(1) and (f)(1)(A). See Pls. Mem. at 7.

As is evident in the plain language of the 1997 Proposed Rule, there is no such thing as the "Consolidated Standard." Nowhere does FDA even suggest that it is *combining* the "injurious to health" analysis with a "significant and unreasonable risk" analysis, much less that such a fictional combination represents "existing policy" for regulating dietary supplements harmoniously with conventional foods. FDA made no attempt to restrict, consolidate with other standards, or otherwise modify the dietary supplement adulteration provision that Congress enacted in § 342(f)(1)(A). Nutraceutical's view that FDA "focused on identifying those dose levels that were both injurious to health and that presented a significant and unreasonable risk of illness or injury" in the 1997 Proposed Rule (Pls. Mem. at 7) is incorrect. Only by repeatedly disregarding the plain words of the Proposed Rule could one conclude that FDA initiated the rulemaking process with a view toward basing a determination of adulteration for EDS on a consolidation of different statutory adulteration standards.

In the 1997 Proposed Rule, FDA "tentatively determined that several measures [were] needed if the observed adverse events associated with the use of [EDS] are to be effectively addressed." 62 Fed. Reg. at 30,692. The measures comprising the agency's proposed regulatory approach for EDS included:

- (1) limiting ephedrine alkaloids to less than 8 mg per serving;
- (2) requiring the label to limit ephedrine alkaloids to an intake of less than 8 mg in a six-hour period and a total daily intake of less than 24 mg;
- (3) requiring the label to state that the product should not be used for more than 7 days;
- (4) prohibiting the use of ingredients with stimulant effects in combination with EDS;

(5) prohibiting label claims that promote long-term use and requiring label claims to state that serious adverse effects may result from short-term excessive use; and

(6) requiring various additional warning statements on the label.

When describing each of these measures in the 1997 Proposed Rule, FDA provided the statutory provisions under which the agency could conclude that EDS were violative if the measures were not implemented. FDA cited to § 342(f)(1)(A), the adulteration standard, as authority for proposed measures 1-4, as stated above. See, e.g., 62 Fed. Reg. at 30,695 (regarding proposed label requirements 1-3); see also id. at 30,696 (regarding proposed prohibition 4).¹⁴

With respect to the proposed per serving limit (measure 1, stated above), the agency tentatively concluded that a finding of adulteration could also be supported by § 342(a)(1) because consuming EDS with 8 mg or more ephedrine alkaloids per serving (i) "may render the dietary supplement injurious to health." 62 Fed. Reg. at 30,963. Nothing in the 1997 Proposed Rule, however, suggests that FDA was proposing to regulate EDS under a "Consolidated Standard."¹⁵ Rather, the 1997 Proposed Rule's citation of two different provisions of the FDCA

¹⁴ Proposed measures 5 and 6 relied on misbranding provisions of the FDCA.

¹⁵ Nutraceutical also asserts that FDA stated in the 1997 Proposed Rule, 62 Fed. Reg. at 30,692, that the "Consolidated Standard" was its "policy." Pls. Mem. at 5, 6. The words "agency's policy" appear within a paragraph discussing the "injurious to health" adulteration standard for regulating a toxin, histamine, in fish. The paragraph reads:

In other cases, where a substance contained in a food may be harmful to health, it has been the agency's policy to define a level at which the harmful substance may render the food adulterated. For example, to address the public health problem of histamine poisoning associated with the consumption of certain fish, the agency issued guidance on the level of histamine at which FDA is likely to take action against the fish because it is adulterated (Ref. 151). Moreover, in § 109.4(b) (21 CFR 109.4(b)), the agency has said that it will establish regulatory limits that represent the

as authority for the proposed restrictions on EDS simply reflects the common and prudent practice of citing all applicable grounds for agency action in rulemaking proceedings. After reviewing all of the information in the record, FDA chose to base the Final Rule on the adulteration standard that it determined was best suited to protect the public health against the adverse health effects associated with EDS use.

The fact that the "Consolidated Standard" never existed renders moot Nutraceutical's argument that FDA did not follow this standard that it allegedly proposed in 1997. In Nutraceutical's view, FDA should have provided notice and an opportunity to comment on the "startlingly complete substantive break" (Pls. Mem. at 11) revealed in the Final Rule in 2004. Nutraceutical argues that, because FDA did not give such notice and opportunity for comment, and the unreasonable risk standard is not a logical outgrowth of the "Consolidated Standard," the agency violated the APA. However, as already shown, FDA never created a "Consolidated Standard" and, therefore, there can be no departure from it. If the so-called "Consolidated Standard" – imagined by Nutraceutical – were such a "startlingly complete substantive break," it is difficult to understand why Nutraceutical did not raise this issue in its initial brief. In fact, in

level at which an added poisonous or deleterious substance adulterates a food within the meaning of section 402(a)(1) of the act (21 U.S.C. 342(a)(1)).

62 Fed. Reg. at 30,692. As evident from even a cursory reading, nothing in this paragraph supports the existence of a "Consolidated Standard" that amalgamates the "significant or unreasonable risk" standard of § 342(f)(1)(A) with the "injurious to health" standard in § 342(a)(1). In fact, the "significant or unreasonable risk" standard is not even mentioned on the page cited by Nutraceutical.

its comments to the proposed rule, Nutraceutical appears to have taken the opposite view and to have already understood that FDA was applying the standard in § 342(f)(1)(A).¹⁶

Moreover, Nutraceutical is incorrect in its contention that, because FDA stated in the Final Rule that it was using the unreasonable risk standard for the *first* time, the use of this standard represents a departure from the 1997 Proposed Rule. See Pls. Mem. at 9-10. The agency's point, as spelled out in the Final Rule, was simply that FDA had not previously removed products from the market under the dietary supplement adulteration provision added by DSHEA. See 69 Fed. Reg. at 6794 (stating that the agency is using its "rulemaking authority for [EDS] because [FDA is] articulating a standard for unreasonable risk under 402(f)(1)(A) of the act [§ 342(f)(1)(A)] for the first time and because it is more efficient to declare these products adulterated as a category than to remove them from the market in individual enforcement actions"). Thus, the 1997 Proposed Rule (and the Final Rule) represents the agency's first use of the new provision added by DSHEA.

Nutraceutical also argues that FDA's use of the phrase "significant and unreasonable risk" in the 1997 Proposed Rule when discussing the § 342(f)(1)(A) "significant or unreasonable risk" adulteration provision establishes that the agency initially interpreted that provision as containing only one adulteration standard, not two. Thus, according to Nutraceutical, the Final Rule's reliance on only the "unreasonable risk" part of the provision was a new interpretation not

¹⁶ See, e.g., Nutraceutical's Comments (Apr. 7, 2003) at 4, 5, respectively (attached to Pls. Mem. at Exhibit C) (stating that (i) the "first step in the process of determining whether any dietary supplement product meets this standard [21 U.S.C. § 342(f)(1)(A)]" is to define "'significant risk'" and "'unreasonable risk,'" and (ii) there is "no basis for a determination" that Nutraceutical's EDS product "present a 'significant or unreasonable risk of illness or injury'"). These comments belie the notion that Nutraceutical believed FDA was proceeding under the "Consolidated Standard" and was surprised by the Final Rule's reliance on § 342(f)(1)(A).

foreshadowed in the 1997 Proposed Rule. See Pls. Mem. at 6, 8 n.4. Once again, Nutraceutical misconstrues the agency's thoroughness in citing all applicable grounds for the regulatory measures in the 1997 Proposed Rule as a binding statutory interpretation.

When articulating the § 342(f)(1)(A) adulteration standard in the 1997 Proposed Rule, FDA consistently refers to it as "significant or unreasonable risk." 62 Fed. Reg. at 30,693, 30,704, 30,705 (emphasis added). It is only in the 1997 Proposed Rule's tentative conclusions about EDS being adulterated under § 342(f)(1)(A) absent the proposed restrictions that the agency uses the "significant and unreasonable" language. See, e.g., 62 Fed. Reg. at 30,695, 30,696, 30,698. As with FDA's citation to both § 342(f)(1)(A) and § 342(a)(1) as legal authority for the proposed restrictions, the agency was simply expressing its tentative conclusion that EDS that did not meet the proposed regulatory restriction would be adulterated under both the "significant" and "unreasonable" prongs of § 342(f)(1)(A), not opining that "significant" and "unreasonable" have the same meaning. The FDCA is clear that "unreasonable risk" has a meaning independent from "significant risk," and Nutraceutical's argument that FDA erred in the Final Rule by not giving regard to "significant" (Pls. Mem. at 9) was defeated on appeal. Nutraceutical, 459 F.3d at 1039-40.

B. FDA's Interpretation That Unreasonable Risk Requires A Risk-Benefit Analysis Is Not A Substantive Rule

Nutraceutical is also misguided in arguing that FDA's risk-benefit analysis is a substantive rule, which "could not have been legally adopted except by following the familiar notice-and-comment procedures of the APA."¹⁷ Pls. Mem. at 11. Nutraceutical focuses on

¹⁷ A substantive rule, which is subject to the notice-and-comment rulemaking requirements, "establishes a standard of conduct which has the force of law." American Mining Congress v. Marshall, 671 F.2d 1251, 1263 (10th Cir. 1982) (quoting Pacific Gas & Electric Co.

FDA's use of the word "standard" in the Final Rule as if it were synonymous with "substantive rule." Pls. Mem. at 9-10. However, Nutraceutical errs by conflating the agency's interpretation of a clear statutory standard with its application of the standard to EDS through rulemaking. Further, to the extent that Nutraceutical's contentions in this regard are actually re-arguments of the statutory meaning of "unreasonable risk," they must be rejected in light of the Tenth Circuit's recent decision.

FDA interpreted and implemented the "unreasonable risk" adulteration standard in the Final Rule. By interpreting "unreasonable risk" to require a risk-benefit analysis, FDA neither established a new standard of conduct not already set forth in existing law nor imposed any new requirements apart from those already imposed by Congress in the FDCA. Nutraceutical, 459 F.3d at 1038 ("The plain language of the statute directs the FDA to restrict distribution of dietary supplements which pose any risk that is unreasonable in light of its potential benefits."). The only substantive rule at issue here is the Final Rule, which concluded that EDS are adulterated and, therefore, can no longer be marketed. The Final Rule marks the culmination of the agency's decision-making process, has the force of law, and was subject to the APA's notice and comment requirements, with which FDA complied.

The cases cited by Nutraceutical in support of its view that FDA's interpretation of "unreasonable risk" is a substantive rule are unavailing. See Pls. Mem. at 11-12 (citing Beirne v. Sec'y of Dep't Agric., 645 F.2d 862 (10th Cir. 1981); United States v. Seward, 1981 U.S. App. LEXIS 21300 (10th Cir. 1981); and Center for Auto Safety v. NHTSA, 452 F.3d 798 (D.C. Cir. 2006)). Indeed, in Seward, the court *distinguished* a substantive rule it was reviewing from an

v. Federal Power Comm'n, 506 F.2d 33, 38 (D.C. Cir. 1974)); see Ballesteros v. Ashcroft, 452 F.3d 1153, 1159 (10th Cir. 2006).

"agency interpretation of law." 1981 U.S. App. LEXIS *14. Moreover, in Center for Auto Safety, the court reviewed whether agency guidelines should be characterized as a binding rule and stated that "the case law is clear that we lack authority to review claims under the APA where an agency merely expresses its view of what the law requires of a party, even if that view is adverse to the party." 452 F.3d at 808 (internal quotations omitted). Finally, Beirne is not relevant to Nutraceutical's point. See 645 F.2d at 865 (holding, where the final regulation varied from the proposed regulation, that the "bare words of the proposal were adequate to alert" interested parties).

Cases not mentioned by Nutraceutical further defeat its claim. FDA's interpretation of "unreasonable risk" is "within the agency's inherent authority to interpret terms in statutes over which it has enforcement authority." Kaw Valley, Inc. v. EPA, 844 F. Supp. 705, 710 (D. Kan. 1994). "Mere interpretations of language are not subject to . . . the notice and comment procedure under 5 U.S.C. § 553" Id. at 710-11; see also York v. Sec'y of Treasury, 774 F.2d 417, 420 (10th Cir. 1985) (holding, in a challenge to agency adjudication, that the portion of the agency's ruling interpreting statutory language was not subject to the notice-and-comment requirements of the APA); Fertilizer Inst. v. EPA, 935 F.2d 1303, 1308 (D.C. Cir. 1991) ("as a general rule, an agency can declare its understanding of what a statute requires without providing notice and comment"); Cf. Mission Group Kansas, Inc. v. Riley, 146 F.3d 775, 783-85 (10th Cir. 1998) (noting that, if the court found that the agency's rule was an interpretation of its governing statute, the APA's notice-and-comment procedures would not apply).¹⁸ Thus, FDA's

¹⁸ See also Reno-Sparks Indian Colony v. EPA, 336 F.3d 899, 909-910 (9th Cir. 2003) (holding that an explanation of agency's interpretation of a pre-existing statute did not constitute a substantive rule requiring notice and comment).

interpretation of the "unreasonable risk" standard set forth at 21 U.S.C. § 342(f)(1)(A) does not constitute a separate substantive rule requiring separate notice and comment under the APA.¹⁹

Even if notice and opportunity for comment were required for an agency's interpretation of its statute, in light of the Tenth Circuit's holding that "Congress unambiguously required the FDA to conduct a risk-benefit analysis under DSHEA" (Nutraceutical, 459 F.3d at 1038), there would be no need for FDA to give notice to the public of its interpretation here because the statutory provision is plain on its face. As also noted by the Tenth Circuit, FDA correctly interpreted the statute and "followed the congressional directive to analyze the risks and benefits of EDS in determining that there is no dosage level of EDS acceptable for the market." Id. at 1043.

C. The Final Rule Is Not Arbitrary Or Capricious

Finally, Nutraceutical's argument that the Final Rule is arbitrary and capricious ignores the FDCA's statutory scheme. Nutraceutical contends that the Final Rule is arbitrary and capricious because it applies only to dietary supplements, and not to food or drugs. As described above, however, this treatment is consistent with – indeed, required by – the statutory scheme. The adulteration standard contained in 21 U.S.C. § 342(f)(1)(A) applies only to dietary supplements, and not to food or drugs. Accordingly, FDA acted properly in restricting the application of the Final Rule to dietary supplements.²⁰

¹⁹ Indeed, the opposite conclusion would render administrative rulemaking virtually impossible, as agencies would be required to undertake multiple notice and comment procedures every time they attempted to apply a statute – one for the manner in which the agency interprets a statutory provision, and one for the substantive result of that interpretation.

²⁰ Notably, Nutraceutical fails to mention, let alone distinguish, the Tenth Circuit's holding that "FDA was not arbitrary or capricious in its Final Rule." Nutraceutical, 459 F.3d at 1043.

CONCLUSION

For the foregoing reasons, this Court should deny Plaintiffs' Motion for Summary Judgment and grant Defendants' Cross-Motion for Summary Judgment.

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Dated: January 18, 2007

CERTIFICATE OF SERVICE

I hereby certify that on this 18th day of January, 2007, I electronically filed a true and correct copy of "DEFENDANTS' OPPOSITION TO PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT AND MEMORANDUM IN SUPPORT OF CROSS-MOTION FOR SUMMARY JUDGMENT" with the Clerk of the Court using the CM/ECF system which sent notification of filing to the following:

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